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Intensity-modulated radiotherapy, coplanar volumetric-modulated arc, therapy, and noncoplanar volumetric-modulated arc therapy in, glioblastoma: A dosimetric comparison

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ABSTRACT

Objective: Advanced techniques such as volumetric-modulated arc therapy (VMAT) may reduce radiation damage and improve the quality of life for patients.We performed a study comparing dose distributions to the planning target volumes(PTVs) and other organs at risk (OARs) of intensity-modulated radiotherapy (IMRT),coplanar VMAT (coVMAT), and non-coplanar VMAT (ncVMAT).

Patients and methods: 13 patients with GBM who had undergone postoperative radiotherapy were enrolled. Three plans for each patient were created, namely, IMRT, coVMAT, and ncVMAT. Prescription doses and normal-tissue constraints were identical for these three plans. The dosimetric differences of target dose distribution, conformity index (CI), homogeneity index (HI), the gradient index (GI), dose of OARs, monitor units (MUs) and beam-on times among these three plans were investigated.

Results: These three techniques resulted in comparable maximum, minimum, and mean PTV doses. Small but insignificant differences were observed in GI,CI, and HI. Compared with IMRT, VMAT plans showed statistically significant reductions in the mean doses to the optic chiasm ($P < 0.05$). Compared with IMRT, VMAT techniques significantly reduced the number of MUs and less beam-on time than IMRT techniques ($P < 0.05$). However, calculation times were significantly longer for ncVMAT and coVMAT plans at 12 and 12.3 min, versus 2.6 min for IMRT. Our study showed that IMRT or VMAT planning is feasible and efficient for patients with GBM.Compared to IMRT plans, ncVMAT or coVMAT plans showed similar PTV coverage and comparable OARs sparing. VMAT plans significantly reduces the mean doses to the optic chiasm than IMRT plans.

Conclusion: There was no obvious superiority of ncVMAT over coVMAT in target coverage and sparing of OARs.Compared with IMRT, VMAT techniques significantly reduced the number of MUs and beam-on time but extended the calculation times.

1. Introduction

Glioblastoma (GBM) is the most common malignant cranial neoplasm in adults,with a median overall survival (OS) less than two years [1]. A study reported the 5-years survival rate of GBM is only about 5% [2]. The standard treatment of GBM consists of surgery with concomitant chemotherapy and radiotherapy(RT), followed by temozolomide adjuvant chemotherapy.Despite recent advances of novel therapeutic strategies,survival of patients with GBM remains poor [1,2]. Radiotherapy of the brain may cause many adverse reactions such as memory and hearing loss,visual impairment,radiation necrosis, and affect the daily life of patients [3]. It is meaningful to choose the optimal radiation technology to reduce the side effects of radiation while ensuring the effect of radiation.Technical advances,such as intensity-modulated radiotherapy(IMRT) and volumetric-modulated arc therapy (VMAT) have been confirmed as valid treatment alternatives for 3D con-formal radiotherapy(3D-CRT) and might reduce treatment-related side effects in long-term survivors [4–6].VMAT is now becoming a standard of radiotherapy treatment for head and neck cancer [7,8].VMAT plans with single or multiple full or partial arcs are used instead of static multiple beams at different gantry angles and modulation of intensity is achieved by variation of MLC(Muti-Leaf Collimmator) speed, gantry rotation speed and dose rate during the rotation of the gantry [9].The VMAT plans required fewer monitor units (MUs) and reduced treatment delivery duration but prolonged plan optimization times,compared to IMRT plans [7]. Recently,noncoplanar technology in IMRT and VMAT have been found to be useful for treating intra-cranial malignant tumors [7,10].Most of studies have

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demonstrated that non-coplanar radiation can improve treatment plan quality while reducing the doses of organs at risk (OARs) [11,12].Non-coplanar IMRT and non-coplanar VMAT(ncVMAT) plans resulted in lower contralateral temporal lobe dose than coplanar IMRT and VMAT plan for patients with high-grade gliomas.However, there was no significant differences in non-coplanar and coplanar techniques in the target coverage and PTV equivalent uniform doses [7].At present,there are few studies on the radiotherapy of GBM with ncVMAT technology.The aim of our study was to explore whether ncVMAT has advantages in PTV coverage and OAR sparing compared to coVMAT or IMRT plans.The present study was also compared the doses coverage among these three planning systems(IMRT,coVMAT,ncVMAT)and find the best treatment planning system for patients with GBM.

2. Patients and methods

2.1. Patient selection

A total of 13 patients were histologically proven GBM after surgery was retrospectively selected from our hospital between 2014 and 2018.The eligibility criteria were included:(1)non-secondary GBM;(2) initial radiotherapy;(3)underwent maximum reasonable microsurgical resection,and had an immediate postoperative MRI study.A total of 37 patients with GBM received radiotherapy within five years in our department.Among them, a total of 13 patients met the entry requirements.

2.2. Treatment planning

The Eclipse 10 planning system(Varian Medical Systems,Palo Alto, Calif.) was used for treatment planning and dose distribution calculations.IMRT, coVMAT, and ncVMAT plans were created for each of 13 cases.

2.3. Target definition and prescription dose

The prescription dose was 60 Gy in 30 fractions,with contours based on EORTC Protocol 26052_22053 [13].The maximum dose permitted within the PTV was 110%.The minimum volume of the PTV covered by the 95% isodose line was 98%.Gross tumor volume(GTV) was defined as the contrast-enhancing lesion visible with T1-weighted MR-imaging and T2 fluid attenuated inversion recovery(FLAIR)MRI images.GTV was expanded with a 2 cm margin to create clinical target volume (CTV).CTV was expanded with a 0.3 cm margin to create the PTV.OARs such as optic chiasm,brainstem,optic nerves,lenses and so on were contoured following previous recommendations [2,3].The tolerance doses of OARs were based on previous publications [7].

Three plans(IMRT,coVMAT and ncVMAT)were generated for each patient(Fig.1 and Fig.2).The IMRT plans were created using 7 coplanar fields according clinical experience and the plan optimization used the direct-machine parameter optimization.All VMAT plans were calculated as double full arcs.The coplanar VMAT plans consisted of a reverse 360° dual-arc with a maximum dose rate of 600 MU/min.The optimization algorithm was corrected for the air chamber with stepwise resolution.One arc was set up in a clockwise direction from 181° to 179° with a 30° collimator angle;conversely,the second arc was performed in a counterclockwise direction from 179° to 181° with a 30° collimator angle.The ncVMAT plan used the same curvature and collimator angle as the coplanar plan,except that the angle of the couch of one single arc is 330°.

2.4. Evaluation of treatment plans

Dosimetric parameters were calculated and compared for the PTVs and OARs.For the PTVs,the comparison parameters included maximum dose,the homogeneity index (HI),the gradient index (GI),and the conformity index(CI).The HI was defined as follows: HI = (D2-D98)/D50.Where D2 represent the corresponding dose for 2% of the target volume,D98 represent the corresponding dose for 98% of the target volume,and D50 represent corresponding dose for 50% of the target volume.The HI value will be less than 1,and the closer the HI to 0, the better the homogeneity [14].The CI represents the objective measure of how well the distribution of radiation follows the shape of the radiosurgical target:CI = (TVPV × TVPV)/(TV × PV),where TVPV, TV, and PV represent the volume of the target covered by the prescription dose,target volume,and prescription isodose volume,respectively [15].The CI value will be less than 1,and the closer the CI to 1,the better the conformality.The gradient index(GI), which is an evaluation of dose falloff,was calculated as:GI = PV50%/PV,where PV50% denotes 50% of the prescription isodose volume.The higher GI means the better of radiotherapy plan.Doses to OARs and coverage of the PTVs were evaluated by the dose-volume histogram(DVH).To evaluate target coverage,D2,D95,D98,V95,V100,V105,were compared,where Dx was the dose that was computed for a fraction of a target or an organ volume,and Vx was the volume that was irradiated above a designated dose.

2.5. Statistical analysis

The dosimetric differences among these three plans for the 13 patients were analyzed using the Kruskal-Wallis test.The dosimetric differences between the two treatment plans were analyzed using the Wilcoxon rank-sum test.All the statistical tests were two sided,and $P < 0.05$ was considered statistically significant.All the data was analyzed using SPSS (version 22.0,IBM).

3. Results

3.1. Patient characteristics

There were 13cases with GBM enrolled in our study(Table1).There were 7 male patients and 6 female patients.The median age of all the patients was 52 years(range27-70 years).All characteristics of all the patients were summarized in Table 1.The median PTV volume was 356 cm^3 (range111.7-588 cm^3).

3.2. PTV doses

These three techniques resulted in comparable maximum,minimum,and mean PTV doses(Table2).Small but insignificant differences were observed in GI,CI,and HI.Table 2 showed CI of VMAT plans was better than IMRT plans(IMRT0.81 versus VMAT0.85 and ncVMAT0.828, $p > 0.05$).However,HI of VMAT plans was worse than IMRT plans with no no significant differences.D95% and D98% were similar among these three plans(Table2).

3.3. OAR doses

The doses to normal tissues were all within the clinically acceptable range.In addition to the optic chiasm,these three plans showed no significant differences in the doses to the OARs($p > 0.05$,Table3).VMAT plans significantly reduces the mean doses to the optic chiasm than IMRT plans($p < 0.05$,Table3).

3.4. Time comparison

Table4 showed the calculation,beam-on times and MUs for each technique.Compared with IMRT techniques,VMAT techniques significantly reduced the number of MUs and beam-on times($P < 0.001$).However,the calculation times were significantly longer for ncVMAT and coVMAT plans than that of IMRT plans.

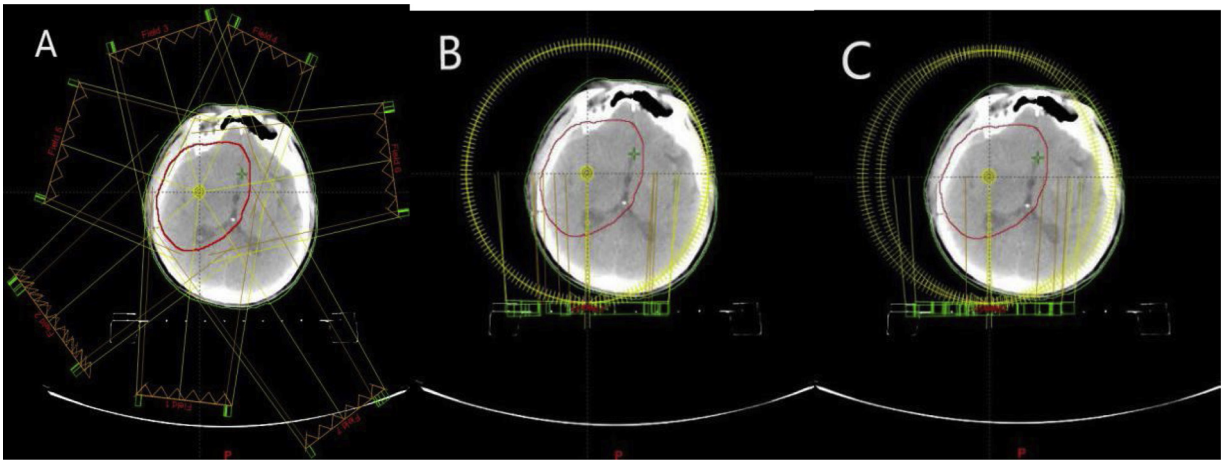

Fig. 1. Cross section of PTV in three plans for one patient. A for IMRT,B for coVMAT,C for ncVMAT.

4. Discussion

VMAT techniques with the variation of gantry rotation speed,beam shaping aperture and delivery dose rate,achieves an IMRT dose distribution with less time than IMRT techniques.Today,VMAT plans usually utilize a coplanar beam trajectory realized by a fixed couch angle,typically 0°.Previous studies have primarily focused on coplanar IMRT or VMAT techniques [6,16].

Compared with IMRT plans,VMAT plans get equal or better coverage of PTV volumes and improved OARs sparing while using fewer MUs and requiring less time to treat high-grade gliomas [7].The faster dose delivery of the VMAT plans can decrease the treatment time and limit the potential for intra-fraction organ and patient motion.The motions can cause unwanted deviations in the dose distribution.However,VMAT plans may need more time for plan optimization [7]. A paper showed that both VMAT and 3D-conformal radiotherapy techniques achieved an adequate doses conformity to the target.The median OS for VMAT patients were significantly longer than patients with 3DCRT(1.56 ± 0.09 years vs 1.21 ± 0.09 years,$P < 0.05$). The median PFS for VMAT patients were also significantly longer than patients with 3DCRT(1.29 ± 0.13years vs 0.99 ± 0.07 years,$P < 0.05$) [17].A study found that there was equivalent PTV coverage,HI,and CI in VMAT and IMRT plans.VMAT significantly reduced maximum and mean retinal,lens,and contralateral optic nerve doses compared with IMRT.IMRT had more MUs and longer treatment times than VMAT plans [7].Wagner et al [16]showed a better target coverage in cases of PTV close to OARs using VMAT compared to VMAT or 3DCRT.VMAT had a shorter treatment time,less MUs and a small V107% than IMRT.VMAT plan provided the best homogeneity coefficient compared to 3D-CRT or IMRT,and had better reduction of mean and maximum dose to OARs and healthy brain than IMRT and 3D-CRT plan [6,18].A study presented the application of coVMAT and coIMRT in treating CNS tumors.VMAT plans reduced maximum dose to chiasm,optic nerves, and cochlea compared with IMRT.The beam-on time of IMRT was significantly longer than VMAT [9].A study also showed the advantage of VMAT over IMRT is lesser MUs and treatment time [19].IMRT resulted in significantly longer delivery times and an

Table 1
Patient characteristics.

Parameter	
Gender	
Male(n)	7
Female(n)	6
Age	
Median(year)	52
Range(year)	27-70
Tumor location	
Frontal lobes(n)	5
Parietal lobes(n)	1
Temporal lobes(n)	3
Fronto-temporal lobes (n)	1
Parieto-temporal lobes (n)	1
Occipitol-temporal lobes(n)	2
Side	
Right(n)	8
Left(n)	5
PTV volume(cm3)	
Median	356
Range	111.7-588

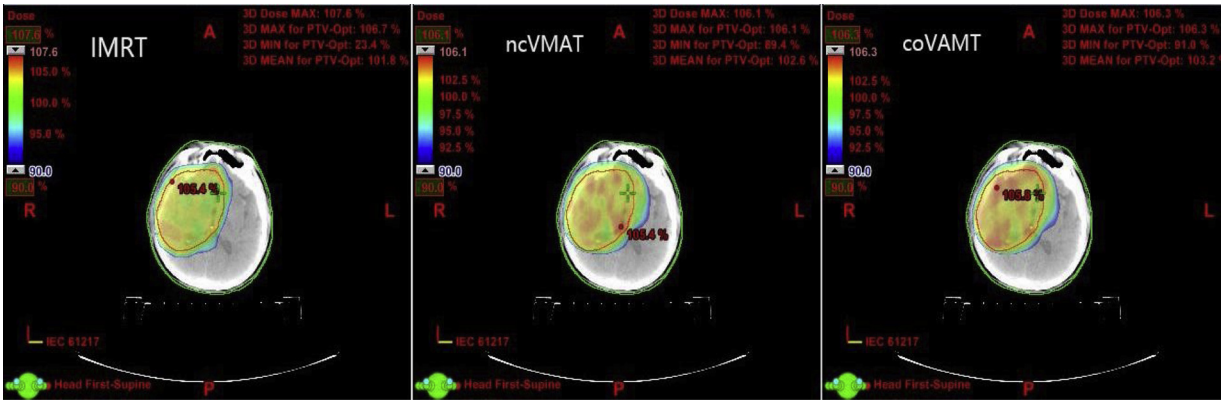

Fig. 2. Comparison of dose distributions in three plans for one patient.

Table 2
Comparison of PTVs dosimetric parameters.

Parameter	IMRT	CO-VMAT	NC-VMAT	Z	P	P1	P2	P3
PTV mean(cGy)	6146	6163	6173	2.147	0.342	0.448	0.153	0.545
PTV max(cGy)	6477	6518	6560	0.684	0.71	0.479	0.92	0.511
PTVmini(cGy)	5182	5219	5268	0.266	0.857	0.88	0.579	0.88
V95%	335	332	334	0.031	0.985	0.88	0.92	0.96
V100%	324	303	318	0.046	0.977	0.84	0.88	0.96
V105%	19.5	16	17.7	0.152	0.927	0.762	0.88	0.762
D2%(cGy)	6296	6328	6329	1.723	0.423	0.448	0.169	0.801
D95%(cGy)	6010	5985	6009	2.39	0.303	0.153	0.479	0.336
D98%(cGy)	5952	5851	5908	5.64	0.6	0.022	0.223	0.186
HI	0.0615	0.0814	0.0731	4.169	0.124	0.064	0.125	0.65
RTOG-CI	0.8098	0.8549	0.8281	3.85	0.146	0.223	0.064	0.448
GI	2.6607	2.8949	2.7889	1.154	0.469	0.243	0.65	0.479

Note:P was the comparison of all the three plans.P1 was the comparison of the IMRT and CO-VMAT.P2 was the comparison of the IMRT and NC-VMAT.P3 was the comparison of the CO-VMAT and NC-VMAT.

increase in MUs when compared to VMAT [18].Wagner et al [16] identified shorter treatment time,fewer MUs, and a small V107% as the major advantages when selecting VMAT techniques over IMRT in malignant glioma cases.In head-and-neck carcinoma cases,VMAT plans had fewer MUs and shorter treatment times while maintaining similar dose distributions,compared to IMRT [20].VMAT plans got higher PTV minimum doses and reduces maximum or mean doses to chiasm and optic nerves,compared to IMRT plan.MUs of VMAT also significantly fewer than IMRT [8].Our study showed that VMAT is superior to IMRT in optic chiasm protection.IMRT resulted in significantly longer beam-on times and increase in MUs compared with VMAT.IMRT had shorter calculation times than coVMAT or ncVMAT plans(Table4).

One study showed that the large number of angles utilized by ncVMAT plans can help improve dose conformity,homogeneity,and organ sparing simultaneously using the same beam trajectory length and delivery time compared to coplanar VMAT plan [6].A paper showed both ncVMAT and coVMAT plans showed superior HI and CI in PTVs compared with IMRT. However,there was no significant difference in CI or HI between ncVMAT and coVMAT plans.Both VMAT plans provided a better protection for OARs than IMRT plans,and ncVMAT plans were superior to coVMAT in sparing of OARs.CoVMAT plans significantly reduced peripheral doses than ncVMAT plans.The both two VMAT plans reduced delivery time than IMRT plans.But the calculation time in VMAT plans was significantly longer than IMRT plans [21].This result was same to our study(table4).NcVMAT plans reduced the mean and maximum doses in OARs compared to coVMAT plans.Compared to ncIMRT or coIMRT plans,both ncVMAT or coVMAT techniques required fewer MUs but longer optimization times and calculation times.This study showed all the four techniques achieved comparable target coverage.Superior sparing of contralateral optic structures was seen with ncIMRT [7].Although VMAT is time consuming,the advantage of reducing treatment time is beneficial to the patients'comfort.A recent study showed coVMAT and ncVMAT achieved similar PTV doses,HI and CI.Compared to coIMRT

Table 3
OAR dose statistics comparison (n = 13).

Parameter	IMRT	CO-VMAT	NC-VMAT	P	P1	P2	P3
Brainstem							
D mean	3232.7	3622	3717	0.663	0.243	0.39	0.84
D max	6385	6442	6445	0.663	0.223	0.204	0.98
Brain							
D mean	3232.7	3622	3717	0.459	0.228	0.369	0.817
D max	6385	6442	6445	0.337	0.209	0.204	0.98
Optic chiasm							
D mean	3412	2980.9	2773.4	0.041	0.043	0.0.039	0.762
D max	5118	5137.7	5022.7	0.663	0.762	0.762	0.961
Pituitary							
D mean	2738.5	3313	2755.1	0.902	0.801	0.98	0.687
D max	3597.7	4062.6	2242.3	0.752	0.92	0.511	0.579
Lens							
D mean	377.7	496.4	464.5	0.641	0.362	0.522	0.898
D max	445.8	532.2	532.4	0.671	0.427	0.457	0.98
Left optic nerve							
D mean	1466.2	1767.7	1271.5	0.928	0.724	0.98	0.801
D max	2237.6	2496.9	2251.4	0.902	0.687	0.92	0.88
Right optic nerve							
D mean	1510.3	1803.1	1686.9	0.516	0.418	0.311	0.724
D max	1956.7	2732	2224	0.992	0.98	0.88	0.98
Left hippocampus							
D mean	3520.7	4242.1	3560.5	0.488	0.511	0.96	0.65
D max	5514	4981.2	5136.6	0.902	0.98	0.98	0.96
Right hippocampus							
D mean	4675.4	4880.5	4511.3	0.918	0.701	0.817	0.817
D max	5841.2	6211.6	6181.8	0.564	0.343	0.427	0.663

Note:P was the comparison of all the three plans.P1 was the comparison of the IMRT and CO-VMAT.
P2 was the comparison of the IMRT and NC-VMAT.P3 was the comparison of the CO-VMAT and.
NC-VMAT.

Table 4
Calculation,beam-on times and MUs for each technique.

Parameter	IMRT	CO-VMAT	NC-VMAT	Overal P	P1	P2	P3
Calculation time(mins)	2.6	12	12.3	P < 0.001	P < 0.001	P < 0.001	0.181
Beam-on time (mins)	2.1	0.7	0.73	P < 0.001	P < 0.001	P < 0.001	0.291
Monitor Units	843	281	291	P < 0.001	P < 0.001	P < 0.001	0.343

Note:P was the comparison of all the three plans.P1 was the comparison of the IMRT and CO-VMAT.P2 was the comparison of the IMRT and NC-VMAT.P3 was the comparison of the CO-VMAT and NC-VMAT.

plans,ncVMAT plans significantly reduces doses to the bilateral hippocampus without increasing the doses to normal brain tissue and other OARs [10].

Our study showed that all the three techniques resulted in clinically acceptable plans,with comparable target doses.NcVMAT technology had no dose distribution advantages and normal organ protection advantages compared with coVMAT technology.VMAT plans had higher CI and HI than IMRT plans,but the results were not statistically significant.Tumor locations,PTV volumes,angles of the couch may induce different results.VMAT techniques provided significantly better sparing of the mean doses of optic chiasm than IMRT techniques in our study.Our article has some limitations.Firstly, this is a retrospective study.Secondly, the sample is small.The result still require a larger sample of studies to confirm.Technique of radiotherapy should be individualized,based on patient-specific clinical and dosimetric parameters.

5. Conclusion

Compared to IMRT plans,ncVMAT or coVMAT plans showed similar PTV coverage.VMAT plans significantly reduced the mean dose to the optic chiasm than IMRT plans.Our study did not demonstrate the obvious superiority of ncVMAT over coVMAT in target coverage and sparing of OARs.And there were no differences in plan calculation and delivery efficiency between ncVMAT and coVMAT.Compared to IMRT,VMAT techniques significantly reduced the number of MUs and beam-on time but extended calculation times.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

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